Claims 5 and 15 were rejected as being indefinite in the recitation of the phrase "in particular." Claims 5, 8, and 15 have each been amended to remove the phrase "in particular." The limitations following the phrase "in particular" in claims 5, 8, and 15 have been incorporated into new claims 28, 29, and 30, respectively. In light of the amendment, Applicants respectfully request that the rejection under 35 U.S.C. §112, second paragraph be withdrawn.

Claim 16 was rejected as being indefinite in the recitation of the term "including." Claim 16 has been amended to remove the entire phrase "including the spleen, tonsil or lymph node." The limitations spleen, tonsil, or lymph node have been incorporated into new claim 32. Similarly, claim 9 has been amended to remove the same phrase, and the limitations spleen, tonsil, or lymph node have been incorporated into new claim 31. In light of the amendment, Applicants respectfully request that the rejection under 35 U.S.C. §112, second paragraph be withdrawn.

Claim 26 was rejected as being indefinite in the recitation of the phrase "substantially as hereinbefore described with reference to the figures." Claim 26 has been amended to remove the entire phrase, and to recite the limitation "wherein the electrophoresis pattern of the known sample has a pattern substantially similar to that of type 4 as shown in figure 4." Support for the amendment can be found in Figure 4 and in claim 10. In light of the amendment, Applicants respectfully request that the rejection under 35 U.S.C. §112, second paragraph be withdrawn.

Claim 27 was rejected as being indefinite in the recitation of the phrase "substantially as hereinbefore described." Claim 27 is cancelled herein without prejudice. Accordingly, Applicants respectfully request that the rejection under 35 U.S.C. §112, second paragraph be withdrawn.

Objections to the Specification

Claims 4-10 and 16 were objected to under 37 C.F.R. 1.75 (c) as being in improper form because a multiple dependent claim cannot depend on another multiple dependent claim. Applicants respectfully submit that the multiple dependencies of claims 4-10 were amended in

the Preliminary Amendment dated February 6, 2001. These amendments are reflected in the clean copy of the pending claims submitted herewith as Appendix B. Accordingly, Applicants respectfully request that the objection to the specification be withdrawn.

Rejection under 35 U.S.C. § 102 (b) over Harrington, *et al.*

Claims 1, 2, and 27 were rejected under 35 U.S.C. 102 (b) as being anticipated by Harrington *et al.* (U.S. Patent No. 4,892,814). Applicants respectfully submit that this rejection is overcome by amendment in part and by traversal in part.

Independent claim 1, as amended, is directed to a method for determining what type of PrP^{Sc} protein (also known as the scrapie PrP protein) is present in a sample by comparing the sizes and ratios of distinct PrP^{Sc} isoforms with those of a sample of known PrP^{Sc} type. Claim 2 depends from claim 1. Claim 27 is cancelled.

Harrington *et al.* teaches a method for distinguishing Creutzfeld-Jacob disease from other neurological conditions by examining proteins in cerebrospinal fluid. In this reference, samples of cerebrospinal fluid were taken from patients suffering from a variety of neurological and other medical conditions. The protein content of each sample was examined, and the results were compared to determine whether the presence or absence of particular proteins indicated the presence of a particular condition. Four proteins were found in all patients suffering from Creutzfeld-Jacob syndrome. However, the reference states that these proteins are of unknown origin and are not likely to be PrP^{Sc} proteins. At column 5, line 35, Harrington *et al.* states:

> The relative mass of the cerebrospinal fluid proteins 130 and 131 is similar to that of the PrP 27-30 complex, but the complex has a much more basic pI. An antiserum to PrP 27-30 was used to probe Western blots containing proteins 127, 128, 130, and 131. Since no reactivity was detected, proteins 127, 128, 130, and 131 appear to be different from the scrapie PrP protein.

Thus, the examination of patterns of protein expression in cerebrospinal fluid as taught by Harrington *et al.* does not involve the detection, identification, or typing of PrP^{Sc} proteins.

Applicants respectfully submit that because Harrington *et al.* does not teach methods that involve the typing of PrP proteins, independent claim 1, and claim 2 which depends from claim 1, are not anticipated by Harrington *et al.* Therefore, Applicants respectfully request that this rejection of claims 1 and 2 under 35 U.S.C. 102 (b) be reconsidered and withdrawn.

Rejection under 35 U.S.C. § 102 (b) over Race *et al.*

Claims 1, 3, 13-15, and 26 were rejected under 35 U.S.C. 102 (b) as being anticipated by Race *et al.* (*American Journal of Veterinary Research* (1992) **53**:883-889). Applicants respectfully submit that this rejection is overcome by amendment in part and by traversal in part.

Independent claim 1, as amended, is directed to a method of determining the type of PrP^{Sc} protein present in a sample of a prion or spongiform encephalopathy disease by identifying the sizes and ratios of distinct PrP^{Sc} isoforms with a standard sample of known PrP^{Sc} type. Claim 3 depends from claim 1. Independent claim 13 is directed to a method of identifying a bovine spongiform encephalopathy infection in an animal or a tissue by isolating a prion protein from the animal and identifying the prion protein by digesting the prion protein with proteinase K, subjecting the digested prion to electrophoresis, and examining the ratios of the resulting protein fragments. Claims 14-15 and 26 depend from claim 13.

Race *et al.* teach a method for determining the presence or absence of PrP^{Sc} protein in tissue samples from sheep by Western blotting. The methods taught by Race *et al.* involve using an antibody that specifically binds to a prion protein to detect the presence or absence of the prion protein. Race *et al.* do not address the existence of different types of PrP^{Sc} protein or compare the physical properties of the PrP^{Sc} proteins detected by Western blotting. While the Western blots of protease-treated samples presented in Race *et al.* display protein fragments of varying molecular masses, Race *et al.* does not compare the relative ratios of these protein fragments in isolates of different PrP^{Sc} types.

Applicants respectfully submit that because Race *et al.* do not teach a method that determines the type of PrP^{Sc} protein present in a sample by comparing the physical characteristics of protease fragment size and glycosylation species, independent claim 1, as amended, is not anticipated by Race *et al.* Race *et al.* also do not teach a method that examines the ratios of glycosylated forms of PrP^{Sc} in a sample from a tissue or an animal. Therefore, independent claim 13, and dependent claims 14, 15, and 26, are not anticipated by Race *et al.*

Rejection under 35 U.S.C. § 102 (e)

Claim 27 was rejected under 35 U.S.C. 102 (e) as being anticipated by Pruisner *et al.* (U.S. Patent No. 6,008,435). Claim 27 is cancelled herein. Therefore, Applicants respectfully submit that this ground of rejection should be withdrawn.

Applicants respectfully request reconsideration of the application in light of the amendments and remarks made herein. If the Examiner believes that a telephonic interview would expedite the allowance of the application, the Examiner is invited to contact the undersigned attorney at the number below.

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MARKED COPY OF PENDING CLAIMS
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1. (Once Amended) A method for typing a sample of a prion or spongiform encephalopathy disease the method comprising comparing and identifying similar physicochemical properties of the sample with a standard sample of known PrP^{Sc} type, wherein the physicochemical properties are the sizes and ratios of distinct PrP^{Sc} glycoforms.

2. A method as claimed in claim 1 wherein the standard sample of known PrP^{Sc} type is bovine spongiform encephalopathy or Creutzfelt-Jakob disease.

3. (Once Amended) A method as claimed in claim 1 wherein the comparison of physicochemical properties comprises a comparison of protease resistance, fragment size, and ratio of PrP^{Sc} glycoforms [and/or glycoform ratios].

5. (Twice Amended) A method as claimed in claim 3 wherein the spongiform encephalopathy is mammalian or chicken derived [in particular, bovine, feline, cervine, ovine, human (or other primate-suitably macaque) or murine derived].

6. (Twice Amended) A method as claimed in claim 3 wherein the method comprises the steps of subjecting the sample to digestion by a protease, electrophoresing the result of the digestion step and comparing the resulting pattern of fragment size and ratio of PrP^{Sc} glycoforms of the electrophoresis with a standard electrophoresis pattern of a known PrP^{Sc} type[sample].

8. (Twice Amended) A method as claimed in claim 6 wherein the sample to be typed if mammalian or chicken derived[, in particular derived from a human, (or other primate-suitably macaque) bovine, feline, ovine, cervine, or murine animal].

9. (Twice Amended) A method as claimed in claim 3 wherein the sample to be typed is derived from brain tissue, other central nervous system tissue, a tissue of the lymphoreticular system [(including the spleen, tonsil or lymph node)], cerebrospinal fluid and/or the blood.

15. A method as claimed in claim 13 wherein the animal, and/or tissue, from which the prion is sampled is mammalian or chicken derived[, in particular, human, (or other primate-suitably macaque) bovine, feline, cervine, ovine, or murine derived].

16. A method as claimed in claim 13 wherein the prion is derived from brain tissue, other central nervous system tissue, a tissue of the lymphoreticular system [(including the spleen, tonsil or lymph node)], cerebrospinal fluid and/or the blood.

26. A method for identifying infection in an animal and/or tissue, as claimed in claim 13, [substantially as hereinbefore described with reference to the examples] wherein the electrophoresis pattern of the known sample has a pattern substantially similar to that of type 4 as shown in Figure 4.

27. CANCELLED

28. (New) The method of claim 5, wherein the spongiform encephalopathy is derived of mammalian origin selected from the group consisting of bovine, feline, cervine, ovine, human, primate, and murine.

29. (New) The method of claim 8, wherein the spongiform encephalopathy is derived of mammalian origin selected from the group consisting of bovine, feline, cervine, ovine, human, primate, and murine.

30. (New) The method of claim 15, wherein the spongiform encephalopathy is derived of mammalian origin selected from the group consisting of bovine, feline, cervine, ovine, human, primate, and murine.

31. (New) The method of claim 9, wherein the prion is derived from a tissue of the lymphoreticular system selected from the group consisting of spleen, tonsil, or lymph node.

32. (New) The method of claim 16, wherein the prion is derived from a tissue of the lymphoreticular system selected from the group consisting of spleen, tonsil, or lymph node.